What is claimed is:

1.   A method of generating a set of compounds that
5   modulate the expression of a target nucleic acid sequence
comprising generating a library of nucleobase sequences *in
silico* according to defined criteria.

2.   A method of generating a set of compounds that
10   modulate the expression of a target nucleic acid sequence
comprising evaluating *in silico* a plurality of virtual
oligonucleotides according to defined criteria.

3.   A method of generating a set of compounds that
15   modulate the expression of a target nucleic acid sequence
comprising robotically synthesizing a plurality of defined
oligonucleotide compounds.

4.   A method of generating a set of compounds that
20   modulate the expression of a target nucleic acid sequence
comprising robotically assaying a plurality of
oligonucleotide compounds for one or more desired physical,
chemical or biological properties.

25   5.   A method of generating a set of compounds that
modulate the expression of a target nucleic acid sequence
comprising generating a library of nucleobase sequences *in
silico* according to defined criteria and evaluating *in
silico* a plurality of virtual oligonucleotides having said
30   nucleobase sequences according to defined criteria.

6.   A method of generating a set of compounds that
modulate the expression of a target nucleic acid sequence
comprising evaluating *in silico* a plurality of virtual
35   oligonucleotides according to defined criteria and
robotically synthesizing a plurality of oligonucleotide

compounds corresponding to said plurality of virtual oligonucleodites.

7.   A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence comprising evaluating *in silico* a plurality of virtual oligonucleotides according to defined criteria and robotically assaying a plurality of oligonucleotide compounds corresponding to said virtual oligonucleotides for one or more desired physical, chemical or biological properties.

8.   A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence comprising generating a library of nucleobase sequences *in silico* according to defined criteria and robotically synthesizing a plurality of oligonucleotide compounds having said nucleobase sequences.

9.   A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence comprising robotically synthesizing a plurality of oligonucleotide compounds and robotically assaying said plurality of oligonucleotide compounds for one or more desired physical, chemical or biological properties.

10.   A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence comprising generating a library of nucleobase sequences *in silico* according to defined criteria and robotically assaying a plurality of oligonucleotide compounds having said nucleobase sequences for one or more desired physical, chemical or biological properties.

11.   A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence,

comprising the steps of:

(a) generating a library of nucleobase sequences *in silico* according to defined criteria;

(b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of (a) according to defined criteria; and

(c) robotically synthesizing a plurality of oligonucleotide compounds.

12. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence, comprising the steps of:

(a) generating a library of nucleobase sequences *in silico* according to defined criteria;

(b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of (a) according to defined criteria; and

(c) robotically assaying a plurality of oligonucleotide compounds for one or more desired physical, chemical or biological properties.

13. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence, comprising the steps of:

(a) generating a library of nucleobase sequences *in silico* according to defined criteria;

(b) robotically synthesizing a plurality of oligonucleotide compounds; and

(c) robotically assaying a plurality of oligonucleotide compounds for one or more desired physical, chemical or biological properties.

14. A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence, comprising the steps of:

(a) evaluating *in silico* a plurality of virtual

oligonucleotides according to defined criteria;

(b) robotically synthesizing a plurality of oligonucleotide compounds; and

(c) robotically assaying a plurality of

5   oligonucleotide compounds for one or more desired physical, chemical or biological properties.

15.   A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence,

10   comprising the steps of:

(a) generating a library of nucleobase sequences *in silico* according to defined criteria;

(b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of (a)

15   according to defined criteria;

(c) robotically synthesizing a plurality of oligonucleotide compounds; and

(d) robotically assaying a plurality of oligonucleotide compounds for one or more desired physical,

20   chemical or biological properties.

16.   A method of generating a set of compounds that modulate the expression of a target nucleic acid sequence, comprising the steps of:

25   (a) generating a library of nucleobase sequences *in silico* according to defined criteria;

(b) choosing an oligonucleotide chemistry;

(c) robotically synthesizing a set of oligonucleotide compounds having said nucleobase sequences of step (a) and

30   said oligonucleotide chemistry of step (b);

(d) robotically assaying said set of oligonucleotide compounds of step (c) for a physical, chemical or biological activity; and

(e) selecting a subset of said set of oligonucleotide

35   compounds of step (c) having a desired level of physical, chemical or biological activity in order to generate said

set of compounds.

17.   A method of generating a set of compounds that
modulate the expression of a target nucleic acid sequence,
comprising the steps of:

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     (a) generating a library of nucleobase sequences *in
silico* according to defined criteria;

     (b) choosing an oligonucleotide chemistry;

     (c) evaluating *in silico* a plurality of virtual
oligonucleotides having the nucleobase sequences of (a) and
the oligonucleotide chemistry of (b) according to defined
criteria, and selecting those having preferred
characteristics, in order to generate a set of preferred
nucleobase sequences;

     (d) robotically synthesizing a set of oligonucleotide
compounds having said preferred nucleobase sequences of
step (c) and said oligonucleotide chemistry of step (b);

     (e) robotically assaying said set of oligonucleotide
compounds of step (d) for a physical, chemical or
biological activity; and

     (f) selecting a subset of said set of oligonucleotide
compounds of step (d) having a desired level of physical,
chemical or biological activity in order to generate said
set of compounds.

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18.   The method of claim 4, wherein said step of
robotically assaying said plurality of oligonucleotide
compounds is performed by computer-controlled real-time
polymerase chain reaction or by computer-controlled enzyme-
linked immunosorbent assay.

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19.   The method of claim 1, wherein said target nucleic
acid sequence is that of a genomic DNA, a cDNA, a product
of a polymerase chain reaction, an expressed sequence tag,
an mRNA or a structural RNA.

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20.   The method of claim 1, wherein said target nucleic acid sequence is a human nucleic acid.

21.   A method of identifying one or more nucleic acid
5   sequences amenable to antisense modulation comprising generating a library of antisense nucleobase sequences *in silico* according to defined criteria.

22.   A method of generating a set of compounds that
10   modulate the expression of a target nucleic acid sequence comprising evaluating *in silico* a plurality of virtual oligonucleotides according to defined criteria.

23.   A method of identifying one or more nucleic acid
15   sequences amenable to antisense modulation comprising robotically synthesizing a plurality of antisense compounds.

24.   A method of identifying one or more nucleic acid
20   sequences amenable to antisense modulation comprising robotically assaying a plurality of antisense compounds for one or more desired physical, chemical or biological properties.

25   25.   A method of identifying one or more nucleic acid sequences amenable to antisense modulation comprising generating a library of nucleobase sequences *in silico* according to defined criteria and evaluating *in silico* a plurality of virtual oligonucleotides having said
30   nucleobase sequences according to defined criteria.

26.   A method of identifying one or more nucleic acid sequences amenable to antisense modulation comprising evaluating *in silico* a plurality of virtual
35   oligonucleotides according to defined criteria and robotically synthesizing a plurality of oligonucleotide

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compounds.

27. A method of identifying one or more nucleic acid
sequences amenable to antisense modulation comprising
5   evaluating *in silico* a plurality of virtual
oligonucleotides according to defined criteria and
robotically assaying a plurality of oligonucleotide
compounds for one or more desired physical, chemical or
biological properties.

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28. A method of identifying one or more nucleic acid
sequences amenable to antisense modulation comprising
generating a library of nucleobase sequences *in silico*
according to defined criteria and robotically synthesizing
15 a plurality of oligonucleotide compounds having said
nucleobase sequences.

29. A method of identifying one or more nucleic acid
sequences amenable to antisense modulation comprising
20 robotically synthesizing a plurality of oligonucleotide
compounds and robotically assaying said plurality of
oligonucleotide compounds for one or more desired physical,
chemical or biological properties.

25 30. A method of identifying one or more nucleic acid
sequences amenable to antisense modulation comprising
generating a library of nucleobase sequences *in silico*
according to defined criteria and robotically assaying a
plurality of oligonucleotide compounds having said
30 nucleobase sequences for one or more desired physical,
chemical or biological properties.

31. A method of identifying one or more nucleic acid
sequences amenable to antisense modulation comprising the
35 steps of:
        (a) generating a library of nucleobase sequences *in*

silico according to defined criteria;

    (b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of (a) according to defined criteria; and

5   **(c)** robotically synthesizing a plurality of oligonucleotide compounds.

32. A method of identifying one or more nucleic acid sequences amenable to antisense modulation, comprising the

10 steps of:

    (a) generating a library of nucleobase sequences *in silico* according to defined criteria;

    (b) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of (a)

15 according to defined criteria; and

    (c) robotically assaying a plurality of oligonucleotide compounds for one or more desired physical, chemical or biological properties.

20 **33.** A method of identifying one or more nucleic acid sequences amenable to antisense modulation, comprising the steps of:

    (a) generating a library of nucleobase sequences *in silico* according to defined criteria;

25   **(b)** robotically synthesizing a plurality of oligonucleotide compounds; and

    (c) robotically assaying a plurality of oligonucleotide compounds for one or more desired physical, chemical or biological properties.

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34. A method of identifying one or more nucleic acid sequences amenable to antisense modulation, comprising the steps of:

    (a) evaluating *in silico* a plurality of virtual

35 oligonucleotides according to defined criteria;

    (b) robotically synthesizing a plurality of

oligonucleotide compounds; and

  (c) robotically assaying a plurality of
oligonucleotide compounds for one or more desired physical,
chemical or biological properties.

35. A method of identifying one or more nucleic acid
sequences amenable to antisense modulation, comprising the
steps of:

  (a) generating a library of nucleobase sequences *in
silico* according to defined criteria;

  (b) evaluating *in silico* a plurality of virtual
oligonucleotides having the nucleobase sequences of (a)
according to defined criteria;

  (c) robotically synthesizing a plurality of
oligonucleotide compounds; and

  (d) robotically assaying a plurality of
oligonucleotide compounds for one or more desired physical,
chemical or biological properties.

36. A method of identifying one or more nucleic acid
sequences amenable to antisense modulation, comprising the
steps of:

  (a) generating a library of nucleobase sequences *in
silico* according to defined criteria;

  (b) choosing an oligonucleotide chemistry;

  (c) robotically synthesizing a set of oligonucleotide
compounds having said nucleobase sequences of step (a) and
said oligonucleotide chemistry of step (b);

  (d) robotically assaying said set of oligonucleotide
compounds of step (c) for a physical, chemical or
biological activity; and

  (e) selecting a subset of said set of oligonucleotide
compounds of step (c) having a desired level of physical,
chemical or biological activity in order to generate said
set of compounds.

37. A method of identifying one or more nucleic acid sequences amenable to antisense modulation, comprising the steps of:

    (a) generating a library of nucleobase sequences *in silico* according to defined criteria;

    (b) choosing an oligonucleotide chemistry;

    (c) evaluating *in silico* a plurality of virtual oligonucleotides having the nucleobase sequences of (a) according to defined criteria, and selecting those having preferred characteristics, in order to generate a set of preferred nucleobase sequences;

    (d) robotically synthesizing a set of oligonucleotide compounds having said preferred nucleobase sequences of step (b) and said oligonucleotide chemistry of step (c);

    (e) robotically assaying said set of oligonucleotide compounds of step (d) for a physical, chemical or biological activity; and

    (f) selecting a subset of said set of oligonucleotide compounds of step (d) having a desired level of physical, chemical or biological activity in order to generate said set of compounds.

38. The method of claim 24, wherein said step of robotically assaying said plurality of nucleic acid sequences is performed by computer-controlled real-time polymerase chain reaction or by computer-controlled enzyme-linked immunosorbent assay.

39. The method of claim 21, wherein said nucleic acid sequence is that of a genomic DNA, a cDNA, a product of a polymerase chain reaction, an expressed sequence tag, an mRNA or a structural RNA.

40. The method of claim 21, wherein said nucleic acid sequence is a human nucleic acid.

41.   A computer formatted medium comprising computer readable instructions for identifying active compounds.

42.   A computer formatted medium comprising computer
5   readable instructions for performing the method of any one of claims 1 to 20.

43.   A computer formatted medium comprising computer readable instructions for performing a method of
10   identifying one or more nucleic acid sequences amenable to antisense modulation.

44.   A computer formatted medium comprising computer readable instructions for performing the method of any one
15   of claims 21 to 40.

45.   A computer formatted medium comprising one or more nucleic acid sequences amenable to antisense modulation in computer readable form.

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46.   A computer formatted medium comprising one or more nucleic acid sequences amenable to antisense modulation in computer readable form, wherein said one or more nucleic acid sequences is identified according to the method of any
25   one of claims 21, 22 or 24-40.